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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/729,343	10/16/1996	DOSUK D. LEE		3866

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CLARK & ELBING LLP
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BOSTON, MA 02110

EXAMINER

GOLLAMUDI, SHARMILA S

ART UNIT	PAPER NUMBER
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1616

DATE MAILED: 08/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

08/729,343

Applicant(s)

LEE ET AL.

Examiner

Sharmila S. Gollamudi

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 April 2005.
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3,7,9-16 and 25 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 1,3,7,9-16 and 25 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____

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DETAILED ACTION

Receipt of Amendments and Remarks received on April 6, 2005 is acknowledged. Claims 1, 3, 7, 9-16, and 25 are pending in this application.

Claim Rejections - 35 USC § 112

The rejection of claims 1, 3, 7, and 9-16 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendment of 4/6/05.

Claim Rejections - 35 USC § 102

The rejection of claims 1, 3, 7, 9-16, and 25 under 35 U.S.C. 102(e) as being anticipated by US patent 5,782,971 to Constantz et al is withdrawn in view of the applicant's arguments of 4/6/05.

Claim Rejections - 35 USC § 103

The rejection of claims 1, 3, 7, 9-16, and 25 under 35 U.S.C. 103(a) as being unpatentable over US patent 5,782,971 to Constantz et al is withdrawn.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

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The rejection of claims 1, 3, 7, 9-16, and 25 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 6,214,368, claims 1-2 of U.S. Patent No. 6,132,463, claims 1-21 of U.S. Patent No. 6,027,742, claims 1-9 of U.S. Patent No. 6,331,312 are maintained for the reasons set forth in the Office Action of April 23, 2003.

Response to Arguments

Applicant states that upon allowance of the instant claims, the applicant may consider filing of a Terminal Disclaimer to overcome the rejection.

Accordingly, the rejection is maintained.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claim 25 under 35 U.S.C. 102(b) as being anticipated by RE 33,221 to Brown et al is maintained.

Brown et al disclose a dental restorative cement pastes. The cements are used for conventional purposes, i.e. to fill a tooth socket, a replacement cone, a cement for implanting and replanting teeth, a material which promotes bone growth, etc. see column 9, lines 20-40. The composition is a mixture of two sparingly soluble calcium phosphates and a dilute aqueous solution. The combination hardens into dental cement when contacted with living tissue. See abstract. The CaP mix contains tetracalcium phosphate and at least one sparingly soluble calcium phosphate, i.e. dicalcium phosphate dehydrate or brushite. See column 3, lines 35-50. The composition may be in a slurry, gel, cement, or injectable form. See example 3. Table II provides the instant setting times. Brown et al disclose methods of manipulating setting times by adding a sizable amount of hydroxyapatite seed crystals to the paste to facilitate crystal formation.

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Further, crystal habit modifiers such as magnesium, citrates, or phosphonates may be used to promote expansion and adhesion. These modifiers absorb onto the specific sites of the crystal surfaces during growth affecting the morphology of the crystals. Further, appropriate combinations of varying particle sizes promote setting expansion. See column 9, line 55 to column 10, line 5. Example 3 further teaches the manipulation of the setting time. The rate of remineralization may also be adjusted which affects the body's ability to resorb the material. Therefore rapid mineralization is beneficial under some circumstances such as incipient dental caries and lesions. Slow mineralization is beneficial for deep lesions. See column 8, lines 25-47.

Response to Arguments

Applicant argues that Brown does not teach or suggest a PCA calcium phosphate product for embedding a prosthesis. Applicant argues that Brown teaches preparing a hydroxyapatite composition and thus all the limitations of the claims are not met.

Applicant's arguments filed 4/6/05 have been fully considered but they are not persuasive. The examiner points to the instant specification on page 7 discloses that a PCA calcium phosphate has **substantially** the same X-ray diffraction spectrum as bone. The examiner points out that Brown on column 9, lines 5-6 discloses the paste hardens to a "bone like consistency". Therefore, since Brown teaches the same components that form the paste and harden within the same time, applicant's claims read on Brown's disclosure, it is the examiner's position that Brown's bone like implant reads on the instant PCA product, the only difference is in that applicant uses the term "PCA" and the prior art's use of "hydroxyapatite".

Accordingly, the rejection is maintained.

Claim Rejections - 35 USC § 103

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The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The rejection of claims 1, 3, 7, 9-16, and 25 under 35 U.S.C. 103(a) as being unpatentable over WO 94/02412 to Simkiss et al is maintained.

Simkiss et al teach an amorphous calcium phosphate that hardens to form bone in vivo. See abstract. The precursor material is applied to the site where bone growth is required. See page 3. Simkiss teaches hydroxyapatite $\text{Ca}_5(\text{OH})(\text{PO}_4)_3$ on page 1 as the inorganic material of choice. The molar ratio of Ca to P is 1.67. Tricalcium phosphate is also taught which has a molar ratio of 1.5. Negligible amounts of magnesium in the composition (as low as 0.001 moles for 1 mole calcium). It should be noted that compositions containing hydroxyapatite or tricalcium phosphate having magnesium and tricalcium phosphate are known to be resorbable. Simkiss exemplifies a material wherein the material is hardened after "many hours". See page 4. However, Simkiss also teaches the ability to modify the transformation rates when the material

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is exposed to body fluid, by including crystallization inhibitors such as pyrophosphate or magnesium ions in certain proportions. See page 2, last paragraph. Simkiss teaches the precursor material contains the inhibitors in low levels, which inhibit the crystallization of the material, and when the implant is in vivo, the inhibitors are leached away by body fluid, thus causing the precursor material to undergo transformation into crystalline hydroxyapatite. See page 3. On page 6, Simkiss teaches transformation time can be controlled by the choice of inhibitor and the choice of inhibitor concentration and/or solubility. A slow mechanism is taught as one requiring natural bone formation and repair mechanism. However, fast-setting material may be used depending on the intended use such as bone filling or bone-grafting. See page 6. X-ray diffraction patterns are seen in Figure 1.

Simkiss does not teach the recited setting time.

However, it is deemed obvious to one of ordinary skill in the art at the time the invention was made to look to the guidance provided by Simkiss and formulate a fast-setting precursor material. One would have been motivated so depending on the intended use of the implant. For instance, Simkiss teaches the use of fast setting for uses such as bone filling whereas if natural bone formation is desired, one would utilize a slow-setting material. Therefore, the motivation to manipulate the parameters of the prior art depends on the intended use of the implant and treatment plan.

Furthermore, Simkiss provides guidance on how to formulate the desired setting rate by stating that a higher concentration of crystallization inhibitor provides for a slow-rate and less of the inhibitor provides for a fast rate.

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It should be further noted that the instant claims recite “hardened within...” but do not recite the degree of hardness. For instance, Simkiss exemplifies a product that takes hours to completely hardened, however the beginning hardening process could fall within applicant’s range.

Lastly, it should be noted that it is the examiner’s position that since Simkiss teaches similar precursor material without distinction, the functional limitation, i.e. the resorption rate will be implicit. However, if applicant argues otherwise, then the applicant has the burden of proving otherwise.

Response to Arguments

Applicant argues that Simkiss does not teach or suggest the preparation of a PCA calcium phosphate for use of treating a bone defect or embedding a prosthesis. Applicant argues that Simkiss teaches preparing a hydroxyapatite composition and thus all the limitations of the claims are not met.

Applicant's arguments filed 4/6/05 have been fully considered but they are not persuasive. The examiner points to the instant specification (page 5, lines 20-27, page 7, line 14 through page 8, line 17, and page 14, line 12 through page 20, line 15) discloses that an amorphous calcium phosphate is converted into the poorly crystalline apatitic calcium phosphate having the X-ray diffraction spectrum similar to that of bone wherein the spectrum is generally characterized by only two broad peaks in the region of 20-35 degrees with one centered at 26 degrees and the other centered at 32 degrees. This is the same spectrum taught by Simkiss (see Figure 1). Thus, the examiner does not see a patentable distinction between the instant PCA product and that of Simkiss’s product except in the applicant’s use of the term “PCA” and the

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prior art's use of "hydroxyapatite". If applicant asserts there is a distinction, the examiner suggests providing evidence to demonstrate this.

Accordingly, the rejection is maintained.

The rejection of claims 1, 3, 7, 9-16, and 25 under 35 U.S.C. 103(a) as being unpatentable over WO 94/02412 to Simkiss et al by itself or in view of RE 33,221 to Brown et al is maintained.

Simkiss et al teach an amorphous calcium phosphate that hardens to form bone in vivo. See abstract. The precursor material is applied to the site where bone growth is required. See page 3. Simkiss teaches hydroxyapatite $\text{Ca}_5(\text{OH})(\text{PO}_4)_3$ on page 1 as the inorganic material of choice. The molar ratio of Ca to P is 1.67. Tricalcium phosphate is also taught which has a molar ratio of 1.5. Negligible amounts of magnesium in the composition (as low as 0.001 moles for 1 mole calcium). It should be noted that compositions containing hydroxyapatite or tricalcium phosphate having magnesium and tricalcium phosphate are known to be resorbable. Simkiss exemplifies a material wherein the material is hardened after "many hours". See page 4. However, Simkiss also teaches the ability to modify the transformation rates when the material is exposed to body fluid, by including crystallization inhibitors such as pyrophosphate or magnesium ions in certain proportions. See page 2, last paragraph. Simkiss teaches the precursor material contains the inhibitors in low levels, which inhibit the crystallization of the material, and when the implant is in vivo, the inhibitors are leached away by body fluid, thus causing the precursor material to undergo transformation into crystalline hydroxyapatite. See page 3. On page 6, Simkiss teaches transformation time can be controlled by the choice of inhibitor and the choice of inhibitor concentration and/or solubility. A slow mechanism is taught is one required

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natural bone formation and repair mechanism. However, fast-setting material may be used depending on the intended use such as bone filling or bone-grafting. See page 6. X-ray diffraction patterns are seen in Figure 1.

Simkiss does not teach the recited setting time.

Brown et al disclose dental restorative cement pastes. The cements are used for conventional purposes, i.e. to fill a tooth socket, a replacement cone, a cement for implanting and replanting teeth, a material which promotes bone growth, etc. see column 9, lines 20-40. The composition is a mixture of two sparingly soluble calcium phosphates and a dilute aqueous solution. The combination hardens into dental cement when contacted with living tissue. See abstract. The CaP mix contains tetracalcium phosphate and at least one sparingly soluble calcium phosphate, i.e. dicalcium phosphate dehydrate or brushite. See column 3, lines 35-50. The composition may be in a slurry, gel, cement, or injectable form. See example 3. Table II provides the instant setting times. Brown et al disclose methods of manipulating setting times by adding a sizable amount of hydroxyapatite seed crystals to the paste to facilitate crystal formation. Further, crystal habit modifiers (up to 1%) such as magnesium, citrates, or phosphonates may be used to promote expansion and adhesion. These modifiers absorb onto the specific sites of the crystal surfaces during growth affecting the morphology of the crystals. Further, appropriate combinations of varying particle sizes promote setting expansion. See column 9, line 55 to column 10, line 5. Example 3 further teaches the manipulation of the setting time. The rate of remineralization may also be adjusted which affects the body's ability to resorb the material. Therefore rapid mineralization is beneficial under some circumstances such as incipient dental caries and lesions. Slow mineralization is beneficial for deep lesions. See column 8, lines 25-47.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Simkiss et al and Brown et al and manipulate Simkiss's formulation to yield a fast-setting precursor material. One would have been motivated so since Brown et al also teach a calcium phosphate injectable composition that has setting capabilities at physiological temperatures. Further, Brown provides guidance on how to manipulate the setting condition by changing the amount of hydroxyapatite, adding crystal modifiers such as magnesium, phosphonates, and citrates, which also taught by Simkiss for the same purpose of manipulating setting time. Therefore, it can be seen that manipulation of setting times is a conventional practice done in the art at the time the invention was made. Lastly, one would have been motivated to manipulate the parameters of the prior art depending on the intended use of the implant and treatment plan as taught by both Simkiss and Brown et al.

Response to Arguments

Applicant argues that Simkiss and Brown do not teach or suggest the preparation of a PCA calcium phosphate for use of treating a bone defect or embedding a prosthesis. Applicant argues that both Simkiss and Brown teach preparing a hydroxyapatite composition and thus all the limitations of the claims are not met.

Applicant's arguments filed 4/6/05 have been fully considered but they are not persuasive. It is pointed out that in a obviousness rejection, the test for obviousness is not whether the features of the claimed invention is taught in any one reference; rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In instant case, as discussed above the examiner points out that applicant defines PCA as having the X-ray

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diffraction spectrum similar to that of bone wherein the spectrum is generally characterized by only two broad peaks in the region of 20-35 degrees with one centered at 26 degrees and the other centered at 32 degrees. This is the same spectrum taught by Simkiss (see Figure 1). Thus, the only teaching lacking in Simkiss is the instant setting time. Therefore, the examiner relies on Brown for its specific teaching of manipulating setting times of the paste. The combination of Simkiss in view of Brown as a whole suggests the instant invention.

Thus, the rejection is maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.


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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sharmila S. Gollamudi
Examiner
Art Unit 1616

SSG


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